```
      ---  -----  -----------
? s (tumor? or cancer? or malignan?) (5n) (cell(w)line??)
Processing
         1508425  TUMOR?
         1174877  CANCER?
          472958  MALIGNAN?
         4513960  CELL
         2446750  LINE??
      S1   98795  (TUMOR? OR CANCER? OR MALIGNAN?) (5N) (CELL(W)LINE??)
? s her(w)2 or neu or erb(w)2
Processing
           90118  HER
        10040468  2
            5752  HER(W)2
           13184  NEU
            3989  ERB
        10040468  2
             602  ERB(W)2
      S2   14666  HER(W)2 OR NEU OR ERB(W)2
? s s1 and s2
           98795  S1
           14666  S2
      S3    1415  S1 AND S2
? s ctl??
      S4   36430  CTL??
? s s3 and s4
            1415  S3
           36430  S4
      S5      72  S3 AND S4
? rd
>>>Duplicate detection is not supported for File 340.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
      S6      34  RD (unique items)
? s s6 and py<=1995
Processing
              34  S6
        27411514  PY<=1995
      S7       7  S6 AND PY<=1995
? t s7/3,k,ab/1-7

 7/3,K,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08672829   96025911   PMID: 7594611
  Tumor-specific  and  HLA-A2-restricted  cytolysis  by  tumor-associated
lymphocytes in human metastatic breast cancer.
  Linehan D C; Goedegebuure P S; Peoples G E; Rogers S O; Eberlein T J
  Department  of  Surgery,  Brigham  and  Women's Hospital, Harvard Medical
School, Boston, MA 02115, USA.
  Journal  of  immunology  (Baltimore,  Md. : 1950) (UNITED STATES)   Nov 1
1995,  155  (9)  p4486-91,  ISSN 0022-1767   Journal Code: 2985117R
  Contract/Grant No.: CA 09535; CA; NCI; CA606662; CA; NCI; RO1 CA45484; CA
; NCI
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  A  tumor-specific  cytotoxic T lymphocyte (CTL) immune response has
been well documented in melanoma, renal cell carcinoma, and ovarian cancer.
Conflicting  evidence  exists  regarding  the  existence  of tumor-specific
CTL  populations  in  breast cancer. Tumor cells and tumor-associated
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lymphocytes (TAL) were isolated from the pleural effusions of six consecutive patients with metastatic breast cancer. After solid-phase anti-CD3 stimulation, TAL cultures were expanded with weekly autologous tumor stimulation and low-dose IL-2 for 3 wk. T cell populations were characterized using flow cytometric analysis and ranged from 49 to 91% CD8+, > 98% CD3+, and < 3% CD16+. Functionally, tumor-stimulated TAL showed tumor-specific recognition of autologous tumor cells (241 +/- 142 LU20/10(7)) and no detectable lysis of autologous fibroblasts, Daudi or K562. Cytotoxicity of TAL against HLA-A2+ allogeneic targets was significantly higher when compared with HLA-A2- **tumor cell lines** (127 +/- 76 vs 6 +/- 18 LU, p = 0.0001). This cytotoxicity against autologous and allogeneic tumor cells was blocked by anti-HLA-A2 mAb and cold HLA-A2+ targets in cold-target inhibition assays. TAL from all HLA-A2+ patients recognized GP2, a known, HER2/**neu** -derived tumor-associated peptide Ag that is HLA-A2 restricted. We have shown that TAL obtained from metastatic effusions of breast cancer patients contain lymphocytes that can recognize and lyse autologous and allogeneic tumor cells in a tumor-specific, HLA-A2-restricted fashion. In addition, tumor-specific TAL derived from breast cancer patients can selectively lyse HLA-A2+ pancreatic and ovarian tumor cell targets, suggesting a common HLA-A2-restricted tumor-associated Ag between these distinct epithelial cancers. Further elucidation of the cell-mediated immune response to breast cancer and the identification of shared TAA could result in the development of broadly applicable vaccine therapies for many cancers.

Nov 1 **1995**,

A tumor-specific cytotoxic T lymphocyte (**CTL**) immune response has been well documented in melanoma, renal cell carcinoma, and ovarian cancer. Conflicting evidence exists regarding the existence of tumor-specific **CTL** populations in breast cancer. Tumor cells and tumor-associated lymphocytes (TAL) were isolated from the...

... of TAL against HLA-A2+ allogeneic targets was significantly higher when compared with HLA-A2- **tumor cell lines** (127 +/- 76 vs 6 +/- 18 LU, p = 0.0001). This cytotoxicity against autologous and allogeneic ...

... cold-target inhibition assays. TAL from all HLA-A2+ patients recognized GP2, a known, HER2/**neu**-derived tumor-associated peptide Ag that is HLA-A2 restricted. We have shown that TAL...

7/3,K,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08626708 95385100 PMID: 7656335

Shared T cell epitopes in epithelial tumors.

Peoples G E; Smith R C; Linehan D C; Yoshino I; Goedegebuure P S; Eberlein T J

Laboratory of Biological Cancer Therapy, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.

Cellular immunology (UNITED STATES) Sep **1995**, 164 (2) p279-86, ISSN 0008-8749 Journal Code: 1246405

Contract/Grant No.: CA09535; CA; NCI; R01 CA45484; CA; NCI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We have previously shown the importance of human leukocyte antigen (HLA)-A2 and the proto-oncogene HER2/**neu** in the T cell recognition of ovarian cancer. Since these proteins are ubiquitously expressed in epithelial-derived tumors, we have acid-eluted HLA-bound peptides from ovarian cancers, fractionated the peptides, and reconstituted T cell epitopes on the HLA-A2+ T2 **cell line** to determine if common **tumor**-associated antigens exist among HLA-A2+, HER2/**neu** +

epithelial cancers. We demonstrate that tumor-specific cytotoxic T lymphocytes (**CTL**) generated from tumor-infiltrating lymphocytes isolated from three ovarian, two breast, and two non-small-cell lung cancers recognize at least three of the same peptide fractions from multiple elutions. One of these peptide fractions coelutes with a HER2/**neu**-derived peptide which has been shown recently to be recognized by these same **CTL** . . These findings demonstrate that a common peptide-based tumor vaccine is theoretically possible for many different epithelial-derived cancers.

Sep **1995**,
... previously shown the importance of human leukocyte antigen (HLA)-A2 and the proto-oncogene HER2/**neu** in the T cell recognition of ovarian cancer. Since these proteins are ubiquitously expressed in...

... ovarian cancers, fractionated the peptides, and reconstituted T cell epitopes on the HLA-A2+ T2 **cell line** to determine if common **tumor**-associated antigens exist among HLA-A2+, HER2/**neu** + epithelial cancers. We demonstrate that tumor-specific cytotoxic T lymphocytes (**CTL**) generated from tumor-infiltrating lymphocytes isolated from three ovarian, two breast, and two non-small...

... same peptide fractions from multiple elutions. One of these peptide fractions coelutes with a HER2/**neu**-derived peptide which has been shown recently to be recognized by these same **CTL**. These findings demonstrate that a common peptide-based tumor vaccine is theoretically possible for many...

7/3,K,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08147112 94282743 PMID: 7912166
HER2/**neu**-derived peptides are shared antigens among human non-small cell lung cancer and ovarian cancer.
Yoshino I; Goedegebuure P S; Peoples G E; Parikh A S; DiMaio J M; Lyerly H K; Gazdar A F; Eberlein T J
Division of Surgical Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115.
Cancer research (UNITED STATES) Jul 1 **1994**, 54 (13) p3387-90, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: ROI CA09535; CA; NCI; ROI CA45484; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Previously, we have reported a correlation between the expression of HER2/**neu** and sensitivity to HLA-A2-restricted cytotoxic T-cells (**CTL**) in ovarian cancer. To investigate the role of HER2/**neu** in human non-small cell lung cancer (NSCLC), we established autologous tumor-specific **CTL** from tumor-infiltrating lymphocytes of HLA-A2+ HER2/**neu**+ NSCLC patients. These **CTL** lines specifically recognized HLA-A2+ HER2/**neu** + autologous and allogeneic NSCLC cell lines as well as HLA-A2+ HER2/**neu**+ heterologous ovarian **cancer cell lines**. Furthermore, these **CTL** recognized an overexpressed, HER2/**neu** -derived peptide. From these results, we conclude that HLA-A2 serves as a restriction element in NSCLC. More importantly, at least one HER2/**neu** -derived peptide is a tumor-associated antigen in NSCLC and ovarian cancer.

HER2/**neu**-derived peptides are shared antigens among human non-small cell lung cancer and ovarian cancer.
Jul 1 **1994**,
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HER2/**neu** and sensitivity to HLA-A2-restricted cytotoxic T-cells (**CTL**) in ovarian cancer. To investigate the role of HER2/**neu** in human non-small cell lung cancer (NSCLC), we established autologous tumor-specific **CTL** from tumor-infiltrating lymphocytes of HLA-A2+ HER2/**neu**+ NSCLC patients. These **CTL** lines specifically recognized HLA-A2+ HER2/**neu** + autologous and allogeneic NSCLC cell lines as well as HLA-A2+ HER2/**neu**+ heterologous ovarian **cancer cell lines**. Furthermore, these **CTL** recognized an overexpressed, HER2/**neu** -derived peptide. From these results, we conclude that HLA-A2 serves as a restriction element in NSCLC. More importantly, at least one HER2/**neu** -derived peptide is a tumor-associated antigen in NSCLC and ovarian cancer.

7/3,K,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08052676 94179821 PMID: 8133050
Association of HER2/**neu** expression with sensitivity to tumor-specific **CTL** in human ovarian cancer.
Yoshino I; Peoples G E; Goedegebuure P S; Maziarz R; Eberlein T J
Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115.
Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Mar 1 **1994**, 152 (5) p2393-400, ISSN 0022-1767 Journal Code: 2985117R
Contract/Grant No.: CA 09535; CA; NCI; RO1 CA 45484; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To study potential sources of tumor-associated Ags in human ovarian cancer, we have established two ovarian **tumor cell lines** (OvS1 and OvA2) from two ovarian cancer patients, which express the cellular oncogene HER2/**neu** . Corresponding tumor infiltrating lymphocyte cultures have also been established and display an autologous tumor-specific pattern of cytotoxicity that is HLA-A2 restricted. To determine the potential relationship between HER2/**neu** expression and **CTL** -mediated cytolysis, we first established tumor cell clones from OvS1. These were categorized as high or low expressors of HER2/**neu** (cOvS1+ or cOvS1-, respectively), and cOvS1+ clones displayed a significantly higher sensitivity to **CTL** killing as compared with cOvS1- clones. To modulate the expression of HER2/**neu**, ovarian cancer cells were treated with IFN-gamma. After this exposure, HER2/**neu** expression was significantly decreased, whereas the expression of HLA Class I was significantly increased. Despite the increase in HLA Class I molecules on the cell surface, **CTL**-mediated cytolysis of both OvS1 and OvA2 was significantly decreased. IFN-gamma treated cOvS1+ clones displayed a similar decrease in sensitivity to **CTL** killing, whereas IFN-gamma treated cOvS1- clones displayed an increase or no change in sensitivity to **CTL** . To confirm this apparent association between HER2/**neu** expression and **CTL** recognition, melanoma **tumor cell lines** that were insensitive to ovarian **tumor** -specific **CTL** were transfected with the HER2/**neu** gene. An HLA-A2+ HER2/**neu**-transfected melanoma cell line was made sensitive to HLA-A2 restricted ovarian tumor-specific **CTL** but not to HLA-A2 unrestricted **CTL**, whereas an HLA-A2- HER2/**neu** -transfected melanoma remained insensitive to HLA-A2 restricted **CTL**. These results demonstrate that the sensitivity of ovarian epithelial tumor cells to **CTL** -mediated lysis is associated with the level of expression of HER2/**neu**, suggesting that this oncogene product may serve as a source of tumor-associated Ags or as an inducer of such peptides. This is the first time in a human tumor system that oncogene expression has been related to the induction of antigenicity. These results prompt us to approach new strategies for immunotherapy of cancer.

Association of HER2/**neu** expression with sensitivity to tumor-specific **CTL** in human ovarian cancer.
Mar 1 **1994**,
... potential sources of tumor-associated Ags in human ovarian cancer, we have established two ovarian **tumor cell lines** (OvS1 and OvA2) from two ovarian cancer patients, which express the cellular oncogene HER2/**neu** . Corresponding tumor infiltrating lymphocyte cultures have also been established and display an autologous tumor-specific pattern of cytotoxicity that is HLA-A2 restricted. To determine the potential relationship between HER2/**neu** expression and **CTL** -mediated cytolysis, we first established tumor cell clones from OvS1. These were categorized as high or low expressors of HER2/**neu** (cOvS1+ or cOvS1-, respectively), and cOvS1+ clones displayed a significantly higher sensitivity to **CTL** killing as compared with cOvS1- clones. To modulate the expression of HER2/**neu** , ovarian cancer cells were treated with IFN-gamma. After this exposure, HER2/**neu** expression was significantly decreased, whereas the expression of HLA Class I was significantly increased. Despite the increase in HLA Class I molecules on the cell surface, **CTL**-mediated cytolysis of both OvS1 and OvA2 was significantly decreased. IFN-gamma treated cOvS1+ clones displayed a similar decrease in sensitivity to **CTL** killing, whereas IFN-gamma treated cOvS1- clones displayed an increase or no change in sensitivity to **CTL**. To confirm this apparent association between HER2/**neu** expression and **CTL** recognition, melanoma **tumor cell lines** that were insensitive to ovarian **tumor**-specific **CTL** were transfected with the HER2/**neu** gene. An HLA-A2+ HER2/**neu** -transfected melanoma cell line was made sensitive to HLA-A2 restricted ovarian tumor-specific **CTL** but not to HLA-A2 unrestricted **CTL**, whereas an HLA-A2- HER2/**neu**-transfected melanoma remained insensitive to HLA-A2 restricted **CTL** . These results demonstrate that the sensitivity of ovarian epithelial tumor cells to **CTL**-mediated lysis is associated with the level of expression of HER2/**neu**, suggesting that this oncogene product may serve as a source of tumor-associated Ags or
...
Gene Symbol: HER2/**neu**

7/3,K,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07716673 93238227 PMID: 8097427
Resistance of HER2/**neu** -overexpressing tumor targets to lymphokine-activated-killer-cell-mediated lysis: evidence for deficiency of binding and post-binding events.
Fady C; Gardner A; Gera J F; Lichtenstein A
Department of Medicine, VA Wadsworth-UCLA Medical Center 90073.
Cancer immunology, immunotherapy : CII (GERMANY) May **1993**, 36 (5) p307-14, ISSN 0340-7004 Journal Code: 8605732
Contract/Grant No.: CA 16042; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
HER2/**neu**-overexpressing **tumor cell lines** are relatively resistant to lymphokine-activated killer (LAK) cell cytotoxicity when compared to HER2/**neu**-nonexpressing lines. HER2/**neu** + targets were also resistant to binding by LAK large granular lymphocytes (LGL) as shown by visualization at the single-cell level, a target monolayer binding assay and in "cold" target inhibition experiments. HER2/**neu** + LAK-resistant ovarian cell lines demonstrated an absence of ICAM-1 expression while expression of LFA-3, N-CAM, laminin and beta 1 integrins was comparable to that of HER2/**neu**- targets. In contrast, the HER2/**neu** + breast cell line, SKBR-3, which was also resistant to

lysis and binding by LAK LGL, demonstrated normal expression of ICAM-1. Anti-ICAM-1 antibodies blocked binding and lysis of HER2/**neu** - carcinoma targets by LAK cells, further supporting the notion that lack of ICAM-1 expression on HER2/**neu**+ cells contributes to their resistance. The modest binding and lysis of HER2/**neu**+ targets by LAK cells was significantly inhibited by anti-LFA-1 antibodies, suggesting the existence of another counter-receptor for LFA-1 on HER2/**neu**+ targets. The following also supported deficiencies in post-binding events when HER2/**neu** + cells resisted the lytic activity of LAK cells: (a) when the relative resistance to effector cell binding was overcome by exogenous lectin. HER2/**neu** + cell lines were still resistant to LAK cytolysis, and (b) HER2/**neu** + targets were resistant to perforin-containing granule extracts obtained from the **CTLL**-R8 cytotoxic lymphocyte cell line. These results indicate that deficiency in effector binding as well as post-binding events contributes to the resistance of HER2/**neu** -overexpressing tumor targets to LAK-cell-mediated lysis.

Resistance of HER2/**neu** -overexpressing tumor targets to lymphokine-activated-killer-cell-mediated lysis: evidence for deficiency of binding...
May **1993**,
HER2/**neu**-overexpressing **tumor cell lines** are relatively resistant to lymphokine-activated killer (LAK) cell cytotoxicity when compared to HER2/**neu**-nonexpressing lines. HER2/**neu** + targets were also resistant to binding by LAK large granular lymphocytes (LGL) as shown by...

...single-cell level, a target monolayer binding assay and in "cold" target inhibition experiments. HER2/**neu** + LAK-resistant ovarian cell lines demonstrated an absence of ICAM-1 expression while expression of LFA-3, N-CAM, laminin and beta 1 integrins was comparable to that of HER2/**neu**- targets. In contrast, the HER2/**neu**+ breast cell line, SKBR-3, which was also resistant to lysis and binding by LAK...

... normal expression of ICAM-1. Anti-ICAM-1 antibodies blocked binding and lysis of HER2/**neu**- carcinoma targets by LAK cells, further supporting the notion that lack of ICAM-1 expression on HER2/**neu** + cells contributes to their resistance. The modest binding and lysis of HER2/**neu** + targets by LAK cells was significantly inhibited by anti-LFA-1 antibodies, suggesting the existence of another counter-receptor for LFA-1 on HER2/**neu** + targets. The following also supported deficiencies in post-binding events when HER2/**neu**+ cells resisted the lytic activity of LAK cells: (a) when the relative resistance to effector cell binding was overcome by exogenous lectin. HER2/**neu** + cell lines were still resistant to LAK cytolysis, and (b) HER2/**neu**+ targets were resistant to perforin-containing granule extracts obtained from the **CTLL**-R8 cytotoxic lymphocyte cell line. These results indicate that deficiency in effector binding as well as post-binding events contributes to the resistance of HER2/**neu** -overexpressing tumor targets to LAK-cell-mediated lysis.

7/3,K,AB/6 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04022843 Genuine Article#: RA605 Number of References: 31
Title: IDENTIFICATION OF AN IMMUNODOMINANT PEPTIDE OF **HER-2/NEU** PROTOONCOGENE RECOGNIZED BY OVARIAN TUMOR-SPECIFIC CYTOTOXIC T-LYMPHOCYTE LINES (Abstract Available)
Author(s): FISK B; BLEVINS TL; WHARTON JT; IOANNIDES CG
Corporate Source: UNIV TEXAS,MD ANDERSON CANC CTR,DEPT GYNECOL ONCOL,BOX 67,1515 HOLCOMBE BLVD/HOUSTON//TX/77030; UNIV TEXAS,MD ANDERSON CANC CTR,DEPT GYNECOL ONCOL/HOUSTON//TX/77030; UNIV TEXAS,MD ANDERSON CANC

CTR,DEPT IMMUNOL/HOUSTON//TX/77030
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, **1995**, V181, N6 (JUN 1), P 2109-2117
ISSN: 0022-1007
Language: ENGLISH Document Type: ARTICLE
Abstract: Synthetic peptide analogues of sequences in the **HER-2** protooncogene (**HER-2**) were selected based on the presence of HLA-A2.1 anchor motifs to identify the epitopes on **HER-2** recognized by ovarian tumor-reactive **CTL**. 19 synthetic peptides were evaluated for recognition by four HLA-A2(+) ovarian-specific cytotoxic T lymphocyte (**CTL**) lines obtained from leukocytes associated with ovarian tumors. The nonapeptide E75 (**HER-2**, 369-377:KIFGSLAFL) was efficient in sensitizing T2 cells for lysis by all four **CTL** lines. This peptide was specifically recognized by cloned CD8(+) **CTL** isolated from one of the ovarian-specific **CTL** lines. E75-pulsed T2 cells inhibited lysis by the same **CTL** clone of both an HLA-A2(+) **HER-2**(high) ovarian tumor and a **HER-2**(high) cloned ovarian tumor line transfected with HLA-A2, suggesting that this or a structurally similar epitope may be specifically recognized by these **CTL** on ovarian tumors. Several other **HER-2** peptides were recognized preferentially by one or two **CTL** lines, suggesting that both common and private **HER-2** epitopes may be immunogenic in patients with ovarian tumors. Since **HER-2** is a self-antigen, these peptides may be useful for understanding mechanisms of tumor recognition by T cells, immunological tolerance to tumor, and structural characterization of tumor antigens.

Title: IDENTIFICATION OF AN IMMUNODOMINANT PEPTIDE OF **HER-2/NEU** PROTOONCOGENE RECOGNIZED BY OVARIAN TUMOR-SPECIFIC CYTOTOXIC T-LYMPHOCYTE LINES
, **1995**
Abstract: Synthetic peptide analogues of sequences in the **HER-2** protooncogene (**HER-2**) were selected based on the presence of HLA-A2.1 anchor motifs to identify the epitopes on **HER-2** recognized by ovarian tumor-reactive **CTL**. 19 synthetic peptides were evaluated for recognition by four HLA-A2(+) ovarian-specific cytotoxic T lymphocyte (**CTL**) lines obtained from leukocytes associated with ovarian tumors. The nonapeptide E75 (**HER-2**, 369-377:KIFGSLAFL) was efficient in sensitizing T2 cells for lysis by all four **CTL** lines. This peptide was specifically recognized by cloned CD8(+) **CTL** isolated from one of the ovarian-specific **CTL** lines. E75-pulsed T2 cells inhibited lysis by the same **CTL** clone of both an HLA-A2(+) **HER-2**(high) ovarian tumor and a **HER-2**(high) cloned ovarian tumor line transfected with HLA-A2, suggesting that this or a structurally similar epitope may be specifically recognized by these **CTL** on ovarian tumors. Several other **HER-2** peptides were recognized preferentially by one or two **CTL** lines, suggesting that both common and private **HER-2** epitopes may be immunogenic in patients with ovarian tumors. Since **HER-2** is a self-antigen, these peptides may be useful for understanding mechanisms of tumor recognition...
...Identifiers--MAJOR HISTOCOMPATIBILITY COMPLEX; **CELL-LINES**; EXPRESSION; BINDING; PROTEIN; **CANCER**; HLA-A2; MOLECULES; EPITOPES; RECEPTOR

7/3,K,AB/7 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02077584 Genuine Article#: JY980 Number of References: 25
Title: ENGINEERING A HUMANIZED BISPECIFIC-F(AB')2 FRAGMENT FOR IMPROVED

, BINDING TO T-CELLS (Abstract Available)
Author(s): RODRIGUES ML; SHALABY MR; WERTHER W; PRESTA L; CARTER P
Corporate Source: GENENTECH INC,DEPT PROT ENGN,460 POIN SAN BRUNOBLVD/S SAN FRANCISCO//CA/94080; GENENTECH INC,DEPT PROT ENGN,460 POIN SAN BRUNOBLVD/S SAN FRANCISCO//CA/94080; GENENTECH INC,DEPT MED & ANALYT CHEM/S SAN FRANCISCO//CA/94080; GENENTECH INC,DEPT IMMUNOL/S SAN FRANCISCO//CA/94080
Journal: INTERNATIONAL JOURNAL OF CANCER, **1992**, S7, P45-50
ISSN: 0020-7136
Language: ENGLISH Document Type: ARTICLE
Abstract: We recently constructed a humanized bispecific antibody (BsF(ab')2v1) by separate E. coli expression of each Fab' arm followed by directed chemical coupling in vitro. BsF(ab')2 v1 (anti-CD3/anti-p185HER2) was demonstrated to retarget the cytotoxic activity of human CD3+ **CTL** in vitro against the human breast-**tumor cell line**, SK-BR-3, which over-expresses the p185HER2 product of the proto-oncogene HER2. Our minimalistic humanization strategy is to install as few murine residues as possible into a human antibody in order to recruit antigen-binding affinity and biological properties comparable to that of the murine parent antibody. This strategy proved very successful for the anti-p185HER2 arm of BsF(ab')2 v1. In contrast BsF(ab')2 v1 binds to T cells via its anti-CD3 arm much less efficiently than does the chimeric BsF(ab')2 which contains the variable domains of the murine parent anti-CD3 antibody. Here we have constructed additional BsF(ab')2 fragments containing variant anti-CD3 arms with selected amino acid replacements in an attempt to improve antibody binding to T cells. One such variant, BsF(ab')2 v9, was created by replacing 6 residues in the second hypervariable loop of the anti-CD3 heavy chain variable domain of BsF(ab')2 v1 with their counterparts from the murine parent anti-CD3 antibody. BsF(ab')2 v9 binds to T cells (Jurkat) much more efficiently than does BsF(ab')2 v1 and almost as efficiently as the chimeric BsF(ab')2. This improvement in the efficiency of T-cell binding of the humanized BsF(ab')2 is an important step in its development as a potential therapeutic agent for the treatment of p185HER2 over-expressing cancers.

, **1992**
...Abstract: v1 (anti-CD3/anti-p185HER2) was demonstrated to retarget the cytotoxic activity of human CD3+ **CTL** in vitro against the human breast-**tumor cell line**, SK-BR-3, which over-expresses the p185HER2 product of the proto-oncogene HER2. Our...
...Research Fronts: 1825 002 (C-ERBB-2 ONCOGENE EXPRESSION; EPIDERMAL GROWTH-FACTOR RECEPTORS IN BREAST-CANCER; RAT **NEU** GENE; **HER -2/NEU** AMPLIFICATION PREDICTS POOR SURVIVAL)
90-0293 001 (POLYACRYLAMIDE GELS FOR PROTEIN SEQUENCING; POLYVINYLIDENE DIFLUORIDE MEMBRANES...
?